| Pfizer Inc. | PF-05019702 (PRA-027) |
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| **Mechanism of Action** | Progesterone receptor (PR) antagonist/nuclear receptor 3C3C (NRC3C) antagonist<br>http://iuphar-db.org/DATABASE/ObjectDisplayForward?familyId=98&objectId=627<br>http://www.ncbi.nlm.nih.gov/gene/5241 |
| **Overview** | PF-05019702 is a non-steroidal, selective progesterone receptor (PR) antagonist. Its potency ($IC_{50}$ = 3.1 nM) was determined in antagonist mode, while no PR agonist activity was observed up to 10 µM. In the agonist mode, PF-05019702 had no activity on the estrogen (ER), glucocorticoid (GR), androgen (AR), or mineralocorticoid (MR) receptors up to 10 µM. In the antagonist mode, PF-05019702 had no activity on GR or ER up to 10 µM, but moderate activity on MR ($IC_{50}$ = 2.1 µM) and AR ($IC_{50}$ = 1.1 µM). |
| **Safety/Tolerability** | PF-05019702 was generally safe and well tolerated following doses up to 500 mg QD for 28 days in cycling and postmenopausal women.<br>Nonclinical toxicology data support clinical studies up to 28 days in duration. |
| **Additional Information** | In preclinical studies following oral dosing, PR antagonism by PF-05019702 is distinguished from steroidal PR antagonists by a lack of ovulation inhibition while maintaining PR antagonist activity on reproductive tract endpoints including endometrial thickness, markers of proliferation, and steroid receptor expression. It showed no PR agonist-like activity. |
| **Suitable for and Exclusions** | Clinical studies up to 28 days duration where a PR or PR pathway dependent mechanism has a role in disease. |
| **Clinical Trials** | http://www.clinicaltrials.gov/ct2/results?term=pra-027 |
| **Publications** | http://oasys2.confex.com/acs/236nm/techprogram/P1193440.HTM |